

Howell (1966) notes that diagnosis in geriatric medicine is notoriously difficult. In 40 nonagenarians in South London who came to autopsy, the cause of death was attributed correctly in only 25%. In 35% the diagnosis was partially correct, but in the remaining 40% the fatal lesion was wrongly assigned. In 100 octogenarians the clinical diagnosis was wrong in 50%. He notes the number of diseases which show mental confusion as their chief presenting symptom, the frequency of multiple diseases, and the inability of old patients to give an adequate history.

Wilson (1966) studied the clinical diagnosis in 265 patients of Paddington General Hospital, London, autopsied in 1958. In 139 the diagnosis was clinically 100% right, in 66 it was wrong or missed, in 42 one diagnosis was right and another wrong or missed, and in 18 the diagnosis was clinically 100% wrong.

Holler and De Morgan (1970) compared clinical and post-mortem diagnosis in 200 autopsied patients at Highland Hospital, Rochester, New York. In 52% (104) there was 100% correlation of clinical and autopsy diagnoses and in 40% (80) the major diagnosis was right but the autopsy showed a minor diagnosis was missed or wrong, or gave confirmation of questionable diagnosis or explanation of clinical symptoms. In 8% (16) the major diagnosis was missed.

Marshall (1970) compared the clinical with the necropsy diagnosis for 1000 consecutive coroners' necropsies occurring in 1966-1967 in Northern Ireland. A major diagnostic error was made in 112 cases. No tabulations are given of errors by cause, though some major types of misdiagnosis are discussed.

Burrows (1975) reviewed 252 adult inpatient autopsy protocols

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occurring at Cooper Hospital, Camden, New Jersey in 1973. The major post-mortem findings were essentially the same as the clinical diagnoses in 222 (82.1%), although the autopsy clarified some aspects of the clinical protocol in 122 (48.4%). Malignant neoplasms were found in 113 patients. 87 were correctly diagnosed clinically, 13 were unsuspected clinically and in the remaining 13 the primary site was unidentified or incorrectly identified clinically.

Virkkunen et al (1975) compared the underlying cause and mode of death determined in 600 consecutive cases by forensic physicians before and after medicolegal autopsy in Helsinki in 1967 and 1968. 60 cases were misclassified before autopsy in regard of mode of death (using the five group category natural causes, accident, suicide, homicide and undetermined). The underlying cause of death was incorrectly diagnosed before autopsy in 29.5% (177). 6 of 8 malignant tumours were incorrectly diagnosed.

Cameron et al (1980) set out to determine whether increasing the necropsy rate produced a higher confirmation of clinical diagnosis. 15 consultants from 6 units from hospitals in the Edinburgh area who had participated in a previous study in 1975-1977 (Cameron and McGoogan, 1981a, 1981b, vide infra) were asked to try to obtain permission for necropsy on every death for a period of six months in 1978. This had the effect of increasing the necropsy rate from 30% to 65% and of increasing the rate of confirmation of the main diagnosis to 85% (131/154) from 56% (182/326) in these units. Confirmation of the cause of death was also higher, 58% (90/154) vs.

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18% (60/326). In 121 of the 154 cases in 1978, the clinician was certain about the diagnosis, but the necropsy demonstrated this certainty to be unfounded in 10% (12) of these.

Clark (1981) reviewed 1076 autopsy records during 1974 to 1978, at the National Naval Medical Center, a teaching hospital with an 87% autopsy rate. 9% of these had significant autopsy findings not suspected clinically. 8 patients were stated to have unsuspected tumours (2 of the lung) and 2 to have tumours where the classification was changed following autopsy. The paper does not provide data on the numbers of patients with tumours reported clinically or at autopsy.

Thurlbeck (1981) compared clinical and autopsy diagnoses for 200 patients autopsied at a teaching hospital in Winnipeg in 1978 and 1979. The two sets of diagnoses were compared as regards the major underlying disease, the cause of death, and significant incidental pulmonary findings. There were major disagreements for the major underlying disease in 12% of cases and major disagreements in a further 12%. In only three cases was it considered that different management might have affected the outcome had the correct diagnosis been made during life. There were disagreements as regards the cause of death in 36% of cases, and in 10% of cases the outcome might have been different had the clinical diagnosis been accurate. Major incidental pulmonary findings diagnosed clinically were confirmed in 76% of cases and major pulmonary findings diagnosed at autopsy had been recognized clinically in 83%. No results are cited for lung cancer.

Wheeler (1982) from the University of North Carolina cited

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results of a study involving 286 cases in which 11% showed a significant discrepancy between ante-mortem and post-mortem diagnoses.

Goldman et al (1983) analyzed 100 randomly selected autopsies from each of the years 1960, 1970 and 1980 at a teaching hospital in Boston. Autopsy rates at these three time points were 75%, 71% and 38%. Autopsies revealed major missed diagnoses for which treatment might have resulted in prolongation of survival in 8% of patients in 1960, 12% in 1970 and 11% in 1980. Major missed diagnoses for which treatment would not have been changed were seen in a further 14%, 11% and 10% of patients at the 3 time points. Tumours formed only 9 of these missed diagnoses, 5 in 1960, and 2 each in 1970 and 1980. The authors concluded that "advances in diagnostic technology have not reduced the value of the autopsy" and that "our findings suggest that the current very low autopsy rate in many hospitals is inappropriate and that the autopsy will continue to uncover many shortcomings in both medical and surgical diagnoses".

Scottolini and Weinstein (1983) compared clinical and autopsy diagnosis for 100 adult patients dying at the Kaiser Foundation Hospital, Honolulu in 1979-1982. In 24% the cause of death did not occur in the clinical diagnosis, while in 13% major clinical diagnoses were not confirmed.

Friederici and Sebastian (1984) reviewed the charts and autopsy reports of 2537 patients coming to autopsy in 1973-1982 at a hospital in Illinois. In 244 (10%) of patients, the primary disease as diagnosed at autopsy had not been recognized before death. In 228 (22%) of 1019 patients dying of cancer, the primary site of the

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malignant neoplasm was not known before autopsy. In almost half of these (10%) it was not realized that the patient had a cancer at all. Data were not presented on individual types of cancer.

Gambino (1984), over the period 1978-1982, routinely reviewed all clinical data on 428 patients undergoing autopsy at St Luke's Hospital in New York City before the results of the autopsies were known. No problem was disclosed in 52.6% (225) and in 21.7% (93) there was clarification of a complex case. In 15.6% (67) diagnoses were either missed or made erroneously. In 8.6% (37) the need for a change in medical practice was revealed because treatment was not optimum, and in 1.4% (6) the cases posed major research problems.

Gibinski et al (1985) compared clinical and autopsy diagnosis in 73 patients autopsied at the Silesian Medical School, Katowice, Poland in 1979-1983. A total of 217 diagnoses were made, 147 (68%) confirmed at autopsy, 22 (10%) seen clinically but unconfirmed at autopsy, and 48 (22%) not detected clinically. They note that in an earlier study conducted in 1964-1975 the rate of correct diagnoses was much lower, rising from 29 to 40% over the period.

Schned et al (1986) compared clinical and necropsy diagnosis for 111 autopsies conducted in White River Junction Veterans Administration Medical Center, Vermont in 1983. There was a major disagreement in diagnosis, with a significant impact on therapy or outcome in 14 cases (13%). In a further 10 (9%) cases, major unsuspected diagnoses were uncovered, but deemed not significant enough to have altered the major therapeutic thrust. The authors outline a comprehensive procedure for quality assessment of their autopsy service.

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Stevanovic et al (1986) retrospectively reviewed the findings from 2145 autopsies performed during 1981 to 1984 at the Institute of Pathology at Belgrade University and compared them with the clinical diagnoses. The clinical diagnoses were considered to be completely correct in 48% (1030) of autopsies, partially correct (when one of the principal or secondary diagnoses or the immediate cause of death was missed) in 14% (312), and incorrect or erroneous (when missed diagnoses were of major clinical importance, with direct impact on survival) in 29% (618). A further 9% (185) were unclassified, since the diagnoses had been recorded by the clinicians as probable, uncertain, or open to question. Malignant tumours were found in 525 patients, in 99% of which they were the principal disease. In 58% (307) of these the malignancy had been correctly diagnosed, in 25% (131) the tumour had not been suspected clinically, in 10% (54) the tumour suspected clinically differed from that recorded at autopsy, in 6% (30) what was thought to be the primary site of the malignant neoplasm was found to be a metastatic site, and in 1% (3) only metastases were found at autopsy. The authors noted that the diagnostic inaccuracy had significantly increased between 1981, when over 20% autopsies had been carried out, and 1982-84 when the rate had dropped to around 10%. They attributed this difference "to the fact that by recommending mostly problem cases for autopsy, clinicians are actually referring the cases in which they err the most often, thereby increasing the percentage of incorrect diagnoses".

Battle et al (1987) (the list of authors included Anderson) used Anderson's (1984) method for classifying clinical/necropsy

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discrepancies in a study of 2067 autopsies collected during 1984 from 32 US university and community hospitals, with an average autopsy rate of 29.6%. Based on all 6203 diagnoses, the discrepancy rates by class were 1:7.0%, 2:10.8%, 3:11.9% and 4: 11.1%. Based on the most serious discrepancies per person the rates by class were 1:13.2%, 2:20.6%, 3:15.6% and 4:10.5%. Discrepancy rates were noted to be higher for community than university hospitals, for smaller than larger hospitals, for university hospitals with lower than higher autopsy rates, for older than younger patients, and for females than males. No results were given specific to neoplasms.

Landefeld et al (1988) reviewed clinical diagnoses for 233 autopsies occurring in 1984-1985 at a university teaching hospital and a community hospital in Massachusetts. There were 11% (26) treatable and 14% (33) untreatable major unexpected findings at autopsy. Cancer was identified as a major autopsy diagnosis on 57 occasions, being missed on clinical diagnosis on 2.

Following an earlier study in Bergen in 1975 (Hartveit, 1977 - see section 2.9) comparing clinical and necropsy diagnosis for 742 autopsies, Karwinski and Hartveit (1989) compared diagnoses for a further 833 autopsies in 1984. Agreement was noted on the cause of death in the later sample in 737 cases (88%). For neoplasia, agreement was reached in 330 cases, with 20 false positive and 16 false negative diagnoses. The authors noted that there had been a substantial increase between 1975 and 1984 in the certainty the clinicians attached to their diagnoses, due almost exclusively to an increase in the certainty of the diagnosis of circulatory disease. "Unfortunately, this was not justified as the numbers of false

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positive and false negative diagnoses were high in both years."

Based on a sample of agricultural workers in Hungary first examined in 1964-66 when they were aged 60 or older, Karolyi and Karolyi (1991) compared necropsy records for the 144 persons who had died with death certificates made by attending physicians and by doctor-coroners. The paper was concerned with differences in distribution of causes of death as recorded in the 3 ways and did not give information on numbers of errors. Neoplasms were considered to be the underlying cause of death at necropsy in 25 subjects, by the attending physician in 22 and by the doctor-coroner in 37.

Modelmog et al (1992) describe results from a study carried out in 1987 in Goerlitz, in former East Germany, which was unique in that virtually everyone who died in the municipality in the year, 1023 out of 1060 (96.5%), was autopsied. The authors describe a comparison of underlying cause of death, as determined at autopsy, and as determined from the death certificate, which in this population was based only on the clinical findings. Of the 1023 deaths, there was complete agreement as regards three digit ICD code from the two sources in 540 (53%), minor disagreement (different three digit code, but same broad category) in 180 (18%) and major disagreement (different broad category) in 303 (29%). Neoplasms were seen in 222 autopsies. For these the clinical diagnosis was correct as to site in 138 (62%), correct as to tumour but incorrect as to site (three digit code) in 40 (18%), with the tumour not being detected clinically in 44 (20%). There were a further 21 false positive diagnoses. The authors note their high

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rates of clinical misdiagnosis may be because of the greater proportion of deaths occurring in nursing homes and among the very old in their population.

2.9 Differences between clinical and necropsy diagnoses - studies specifically mentioning lung cancer

2.9.1 Before World War II

Wells (1923) investigated 3712 necropsies, mainly for the period 1917-1922, from Cook County Hospital and the University of Chicago. Among these there were 545 cases of malignant disease. 33% (178) of these had not been recognized as malignant tumours at all. Apart from the 367 cases correctly recognized as malignant tumours, there were an additional 33 cases diagnosed clinically but not found at necropsy. The proportions of internal tumours seen at autopsy than were not recognized clinically (37.1%) was much higher than the corresponding proportion of external tumours. It should be noted that to the 178 cancers not recognized should be added a substantial additional number (I estimate about 70 from partial data provided) where the site of the malignancy was incorrectly diagnosed. Wells provides data on accuracy of diagnosis of the more commonly occurring sites. Of 11 lung cancers only 1 was correctly diagnosed clinically. In 2 cases, the diagnosis was an intrathoracic tumour, in 4 pulmonary tuberculosis and in 1 pneumonia.

Wells (1923) cites results from three earlier studies:

- (i) Reichelmann reported 711 carcinoma cases among a total of 7790 necropsies conducted in Berlin in 1895-1901. 22% (156) were

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not recognized as malignant diseases (regardless of site or tumour type) clinically, while 58 were diagnosed as cancer clinically when this condition was not present.

(ii) Hofmann, based on hospital statistics in Keil, showed an addition of 19.6% to the cancer figure through necropsy.

(iii) Bashford reported 835 cancers found in autopsies conducted in London hospitals. 22% (152) were not recognized as malignant disease at all clinically, while 31 were incorrectly diagnosed as cancer clinically.

Hruby and Sweany (1933) aggregate data from numerous autopsy studies conducted between 1897 and 1930, involving 1355 lung cancers among a total of 185,434 autopsies. They note quite a steady change in the percentage of lung cancers among all autopsies over the period, rising from an average of 0.3% in the first five years (1897-1901) to an average of 1.5% in the last five years (1926-1930).

Rigdon and Kirchoff (1961), in a historical review, note "that the problem of diagnosis of lung cancer was frequently discussed after 1834. By 1930 a marked improvement in the percentage of correct diagnoses had occurred; it was thought to be about 50 per cent correct in the practice of the better physicians, clinics and hospitals". They noted that the number of correct diagnoses had been reported by Ferenzy and Matalusy to be "5 per cent from 1896 to 1900, 28.4 per cent from 1917 to 1925, and 50 per cent in 1925". From the context it appears that the percentages refer to numbers diagnosed clinically as a proportion of numbers seen at autopsy.

Rosenblatt et al (1971a) cite Sehr (1904) as reporting that,

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at the turn of the century, out of 178 cases of lung cancer seen at autopsy only 6 (3.4%) were reported clinically.

Swartout (1934) compared clinical and post-mortem diagnosis of 1805 patients autopsied at New Haven Hospital during the period 1922 to 1933. Of the total number, 89.5% (1615) were correctly diagnosed before death. For respiratory cancer, 20 out of 26 (77%) were correctly diagnosed.

In a further study, Swartout and Webster (1940) compared clinical and post-mortem diagnoses of 8080 patients autopsied at Los Angeles County General Hospital in 1933 to 1937. Overall 78.8% (6365) were correctly diagnosed before death. For respiratory cancer, 71 out of 99 (72%) were correctly diagnosed.

2.9.2 Later studies

Pohlen and Emerson (1942) collected records from ten general hospitals of 4051 autopsied cases in which either upon autopsy, or by clinical statement of cause of death, or in the admission diagnosis to hospital, some form of malignant or unspecified tumour was mentioned. Among these cases were 3462 in which the autopsy report showed some form of malignancy as primary cause of death, and 271 cases in which the malignant tumour, usually in a very early stage, caused no clinical symptoms and was incidentally discovered in the course of the autopsy as a contributory condition. Of the 3462 cases, 2311 were correctly diagnosed clinically as to the existence, nature and site of the tumour. Of 321 lung cancers found to cause death at autopsy, 200 were correctly diagnosed clinically and 134 were also correctly diagnosed at admission to

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hospital. There were in addition 24 lung cancers considered as contributory causes at autopsy, and 12 diagnosed clinically not confirmed at autopsy. Metastases were seen for 81% of lung cancers, and the authors present data about the frequency of involvement of the various sites. Further tabulations are given in Pohlen and Emerson (1943), though these contain no additional information for lung cancer.

Munck (1952) reviewed the clinical diagnosis for 1000 autopsies from the Municipal Hospitals and the Radium Centre in Aarhus. 67 cases had an "incorrect diagnosis" (the principal disease not having been diagnosed at all), 49 had an "inadequate diagnosis" (there being an essential disagreement between the clinical diagnosis and the autopsy findings) and 87 had an "almost correct diagnosis" (the principal disease but not its exact localization had been recognized clinically, or vice versa), resulting in a total of 203 diagnoses that were not correct. In 33 of the 67 cases with an incorrect diagnosis the patient died within the first week after admission. For each specific cancer type (and for various other diseases) Munck presents data on the number found at autopsy, the number not diagnosed clinically and the number with a clinical diagnosis not confirmed. For lung cancer these numbers were, respectively, 20, 6 and 2.

O'Neal et al (1957) carried out various analyses based on all 8183 patients from Barnes Hospital autopsied in the Department of Pathology at Washington University during the years 1910 to 1954. The sections of patients with a diagnosis of carcinoma of the lung were re-examined and the tumours histologically typed, or in 14

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cases reclassified as not being lung cancer. 301 patients with lung cancer remained. The number of lung cancers, as a proportion of total autopsies, rose from 0.7% in 1910-1919 to 5.4% in 1945-54, the rise being more evident in men than women. A correct clinical diagnosis was not made on 7 (100%) of the 68 patients with lung cancer autopsied prior to 1940 and on 40 (17%) of the 233 patients autopsied after 1940. Of the 47 patients, 32 were suspected to have a malignant tumour but not of the lung.

Waalder and Grimstvedt (1958) studied 4104 autopsies occurring in Bergen, Norway during the period 1946-1955 and compared the clinical diagnoses. Of 783 cases of malignant disease seen at autopsy, the clinical diagnosis had been correct in 492. 82 were classed as "doubtful clinical diagnosis", i.e. two or more possible sites of the primary tumour had been discussed but no decision had been taken. 147 were wrongly diagnosed as regards site or presence of tumour. In 49 the malignant tumour found had produced no symptoms or signs and was not the reason for the death (an "incidental finding"), and in 13 the primary site had not been at autopsy. There were 68 cases of cancer of the lung, 33 classed as "correct", 10 as "doubtful", 22 as "wrong" and 3 as an "incidental finding".

Gwynne (1965) based an investigation on 1657 necropsies conducted in various New Zealand hospitals in 1953 to 1964. A total of 447 cancers were discovered among 436 individuals, with cancer of the bronchus being most frequent at 72 cases. Of these 72, 46 were diagnosed correctly clinically, and 26 were diagnosed incorrectly. For 4 of these the primary site had been incorrectly diagnosed, for 7 a malignancy had been diagnosed but the primary

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site had been considered unknown before autopsy, and for 15 no malignancy had been diagnosed. In 19 of the necropsies, malignancy had been diagnosed clinically when none was found at necropsy. 2 of these were misdiagnosed lung cancer.

Heasman and Lipworth (1966) describe a study involving 75 hospitals in England and Wales in 1959. For every patient dying in a 6 month period, a dummy death certificate was completed by a clinician in close clinical contact with the case. Then (providing the relative agreed) an autopsy was to be carried out and a second death certificate completed from the resultant findings. Although in practice only 65% of autopsies were conducted, the percentage varying from 30 to 100% in individual hospitals, data were available for 9501 autopsies and the authors provide voluminous tables on numbers of clinical/autopsy disagreements of various types. For primary lung cancer, there were 227 cases where the autopsy and clinical diagnosis agreed, 190 cases seen only at autopsy, and 111 where the clinical diagnosis was not confirmed by autopsy. Of the 111 false positives, 48 were lung cancer unspecified as to whether primary or secondary by the pathologist, 22 were other neoplasms and 40 other conditions. Of the 190 false negatives, 51 were lung cancer unspecified as to whether primary or secondary by the clinician, 4 were lung neoplasms with malignancy unspecified, 72 were neoplasms of other sites and 62 were other conditions, and 1 was a primary lung cancer differing on the 4th digit of the ICD. The total number of malignant neoplasms of all sites shown as the underlying cause of death was similar in the certificates completed ante-mortem (2281) and post-mortem (2376), but in only 60% of the

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individual cases considered by the clinician to have died of malignant disease was the pathologist in full agreement as to cause and anatomical site. In roughly half of the remainder the death was certified after autopsy to a malignant condition of another site.

In discussion Heasman and Lipworth note that "it is not disputed that a large part of the increase in recorded mortality from cancer of the lung has resulted from improved diagnosis. These data show that there is still considerable room for further improvement, and it is conceivable that this sort of investigation might be repeated and an estimate obtained of how much of the increase was been spurious". They refer to earlier studies, e.g. Gilliam (1955), which made efforts to make allowances for the amount of underdiagnosis, and which made the assumption that the misdiagnosis arose from other respiratory diseases. There is little doubt that this was to a certain extent true in the past, but it is certainly not true now the misdiagnosis occurs firstly with other cancer sites and secondly with cerebro- and cardio-vascular lesions".

Takeda and Kobayashi (1967) extracted cancer cases from a total of 71,922 autopsy cases (15,006 for 1948-1952 and 56,916 for 1958-1962) obtained from all universities and large hospitals in Japan, and compared the clinical diagnosis. For the first period, there were 345 cases of lung cancer seen at autopsy, 48.1% (166) of which were missed. For the seven major cancers considered combined, 41.1% (963/2343) were missed. There were no data for this period on cases seen clinically which turned out not to be lung cancer on autopsy. For the second period, the rate of missed cases had

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decreased somewhat. For the eight major cancers considered combined, 3888 (31.9%) out of 12,180 autopsy cases were missed, and there were an additional 1840 cases seen clinically but unconfirmed by autopsy. For lung cancer, 788 (34.6%) out of 2276 autopsy cases were missed and there were an additional 305 cases only on the clinical report. The paper gives the detailed distribution of which other cancer lung cancers were misdiagnosed with. (N.B. In this study cases of cancer seen only clinically will be underestimated, as those where cancer was not seen at autopsy will be missed.)

Willis (1967) investigated 1000 consecutive necropsies carried out at the Alfred Hospital, Melbourne between 1936 and 1944 in which either a clinical diagnosis of malignant disease had been made or malignant disease was discovered post mortem. The 1000 necropsies comprised 943 actual cases of cancer and 57 cases which had been wrongly diagnosed clinically as cancer. Of the 943 actual cases, 296 had been wrongly diagnosed, 126 as not having cancer at all and 170 as having cancer but the primary site incorrect or unspecified. There were 71 lung cancers proven by autopsy, of which 28 had been wrongly diagnosed, 13 as not cancer and 15 as cancer of a different or unspecified site. There were also 9 cases where a clinical diagnosis of lung cancer was disproved, 4 where some other primary tumour was seen at necropsy and 5 where no malignant tumour was seen.

Rosenblatt et al (1971a) surveyed patients discharged deceased from Doctors' Hospital New York between 1960 and 1969. The discharge diagnoses were reviewed as were autopsy diagnoses where autopsies were carried out. There were 1072 cases in which the

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primary cause of death was certified as some type of malignancy on the basis of clinical diagnosis, 118 of which (11.0%) were classified as cancer of the lung. There were 455 autopsies in which the final diagnosis was some type of malignancy, 25 of which (5.5%) were classified as lung cancer. Of the 118 cases certified clinically, 56 were autopsied, and in 25 cases (45%) the diagnosis was confirmed, the remaining 31 being diagnosed as a tumour of another (or unknown) site. The rate of confirmation of the clinical diagnosis is very much lower than reported by other studies. No cases of lung cancer were found at autopsy but were not clinically diagnosed, again contrasting markedly with results from other studies.

Rosenblatt et al (1971b) extended the study described in Rosenblatt et al (1971a) up to 1971, and considered all autopsies, totalling 1000. Of 139 cases of lung cancer certified clinically, 61 were autopsied and in 27 the diagnosis was confirmed. Again no cases of lung cancer were found at autopsy that were not clinically diagnosed.

Bauer and Robbins (1972) reviewed the clinical diagnosis corresponding to that for 2734 autopsies conducted at the Boston City Hospital, between 1955 and 1965, which had disclosed cancer. Of the total of 3008 cancers seen at autopsy, 797 (26.5%) were clinically undiagnosed. Of 446 lung cancers, 121 were unsuspected clinically and 98 misdiagnosed, a total incorrect of 219 (49.1%). 163 of the 219 were fatal cancers. Bauer and Robbins also present similar data for all the 25 most common malignancies at autopsy. Among the total of 2091 deaths from cancer, 327 (15.6%) were

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undiagnosed and 367 (17.6%) incompletely diagnosed. The authors compared their findings with those of Wells (1923) and concluded that "our study indicates that accurate clinical diagnosis of cancer in municipal hospitals are as much a problem today as they were a half-century ago".

400 deaths occurred during 1970-71 in the Medical Department of Serafimerlasarettet in Stockholm, of which 383 were autopsied. Britton (1974a,b) compared diagnoses made by the same clinicians before and after autopsy. Overall the main cause of death diagnosed clinically was confirmed as correct in 57% of cases and as erroneous in 30%, it not being possible to make a definite diagnosis ante-mortem for the remaining 13%. Of the 113 errors, 28 were considered major, 25 intermediate and 60 minor. Clinical diagnoses of neoplasms were more seldom found to be erroneous than diagnoses of other groups of diseases. Of 50 cases of cancer diagnosed clinically, 48 were confirmed at autopsy, with a further 11 cases seen at autopsy not detected clinically. Of 10 cases of lung cancer diagnosed clinically, 9 were confirmed at autopsy, with a further 7 cases seen at autopsy not detected clinically (3 considered clinically to be cancer of another site, and 4 not to be cancer). The author notes not being able to find any previous studies where diagnosis was made before and after autopsy and where all causes of death are dealt with.

Ehrlich et al (1975) studied 1212 consecutive autopsies of patients who died at the Chaim Sheba Medical Centre in Tel Hashomer, Israel, selecting out for review all with a diagnosis of malignant neoplasm on either the post autopsy record or the pre autopsy

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request form. There were 226 patients confirmed to have cancer, though in 30 there was a discrepancy in the site. There were also 43 cases where the clinical diagnosis was unconfirmed and 28 where the cancer was reported only at autopsy. The false positive and false negative rate increased substantially with age. Of 34 cases of lung cancer, 7 were thought clinically not to have cancer at all, with a further 2 thought to have cancer of another site. 5 cases diagnosed as lung cancer clinically were unconfirmed.

Hartveit (1977) describes results of a study conducted in Bergen in Norway in 1975 in which, for each of 742 autopsies, the clinician had provided a diagnosis together with an opinion as to whether he was certain or uncertain of the diagnosis, and whether he considered it to be essential or desirable. In 19% of the 404 cases where the diagnosis was considered certain, the macroscopic post-mortem diagnosis differed from the clinical diagnosis. In 35% of the 338 cases where the diagnosis was considered uncertain, a difference was seen. Differences in this context were based on the 17 main diagnostic groups of the 8th revision of ICD. For neoplasia, agreement was reached in 173 cases, with 25 false positive clinical diagnoses made and 29 false negative. For lung cancer, agreement was reached in 39 cases, with 4 false positives, and 10 false negatives. The authors point out that "lung cancer is still underdiagnosed, being the most frequent primary site to elude clinical diagnosis". They also suggest that "the idea of selection of cases for autopsy should be replaced by selection of autopsies for microscopic investigation on the basis of the macroscopic

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post-mortem findings, and that "clinicians might profitably attend autopsies on patients in their sphere of interest that were not admitted under their care".

Waldron and Vickerstaff (1977) carried out a survey in the West Midlands and Trent regions of the UK along the lines of the earlier study of Heasman and Lipworth (1966). The underlying cause of death was coded for 1117 decedents both based on clinical data obtained before post-mortem and based on the post-mortem examination. In 531 cases there was complete agreement as to the underlying cause of death, in 295 there was partial agreement (the underlying cause of death clinically appeared on the post-mortem report but not as the underlying cause of death), and in 291 there was disagreement (the underlying cause of death clinically did not appear at all on the post-mortem report). For 244 ante-mortem diagnoses of malignant neoplasms, there were 116 showing complete agreement, 68 partial agreement, and 60 disagreement. The likelihood of ante-mortem and post-mortem diagnoses agreeing diminished with age and with reduced confidence by the clinicians in their initial diagnoses. Of 48 cases where lung cancer was considered to be the cause of death ante-mortem, 77.1% (37) were confirmed by autopsy. There were also 19 cases where lung cancer was considered the cause of death at autopsy and where another cancer had been considered the cause of death ante-mortem. The number where a disease other than cancer had been considered the case ante-mortem is not given.

Hartveit (1979) describes results of a second study in Bergen, this time conducted in 1976 and 1977. The subjects considered include 471 where cancer was considered the cause of death at

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autopsy and 31 where a clinical diagnosis of cancer as the cause of death was not upheld at post-mortem. Of the 471 cases seen at autopsy 72% (337) had a clinical diagnosis agreeing as to the site (ICD A-list), 23% (111) had a clinical diagnosis of cancer but with a differing site, and 5% (27) were considered not to be cancer clinically. Lung cancer was the most common cancer seen at autopsy, with 106 cases. 71 of these were correctly diagnosed clinically, with 30 being diagnosed as cancer not of the lung, and 5 as not cancer. A further 5 cases diagnosed clinically were not confirmed at post-mortem.

Cechner et al (1980) described a study based on 14,074 autopsies carried out over the period 1948 to 1973 in the University Hospitals of Cleveland, Ohio (where a total of 21,950 deaths had occurred). Among these decedents there were 490 cases of lung cancer diagnosed clinically or pathologically, of which 415 were analysed in detail, the clinical records of the remainder being lost or incomplete. The 415 were divided into 260 accurate (primary lung cancer found both at autopsy and clinically), 117 false negative (found at autopsy only) and 38 false positive (clinical diagnosis unconfirmed). Of the 117 false negatives, 82 could have been detected clinically with existing methods, 31 were theoretically detectable and 4 were due to inaccurate judgement based on the data collected. Of the 38 false positives, 23 were classified as doubtful and 15 as due to inaccurate judgement. Cechner et al found that the proportion of all cases found at autopsy for which smoking was reported was similar in cases found at autopsy as in those diagnosed clinically. However, the smoking data were extracted from

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hospital notes and were irregular and non-specific. There was a large proportion of patients with no information on smoking in the notes.

Sandritter et al (1980) compared autopsy and clinical findings in 1096 patients necropsied at the Medical and Surgical Clinics of Freiburg University, where the autopsy rate was 64%. The clinical diagnoses proved to be correct in 36.1% (395), nearly correct in 45.2% (496), inadequate in 16.1% (177), and false in 2.6% (28). Most of the falsely diagnosed patients had stayed in the hospital for a much shorter time than the rest of the patients. Of 324 malignant tumours seen at autopsy, 52 were clinically undiagnosed, and there were a further 18 falsely diagnosed clinically. Of 69 lung cancers seen at autopsy, 60 were clinically diagnosed or suspected.

Cameron and McGoogan (1981a,b) followed the procedures of Heasman and Lipworth (1966) in a study conducted in the South Lothian District of Scotland in 1975-1977. For 1152 deaths for which an autopsy had been carried out, dummy death certificates were completed for both the clinical and autopsy diagnosis. Of the 1152 cases, the underlying cause of death as determined clinically was confirmed in 703 (61%). Even where the clinician was fairly certain or certain about the diagnosis the confirmation rate was only 75% (402/539). Of 320 cases of neoplastic disease considered the underlying cause at autopsy, 109 were not anticipated clinically and there were a further 113 cases where the clinical diagnosis was not confirmed. Of 134 cases of lung cancer diagnosed at autopsy, only 88 were detected clinically. There were also a

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further 15 cases considered to be lung cancer on clinical diagnosis, but disproved at autopsy. Data are also presented for a wide range of other cancers and other diseases.

Gobbato et al (1982) reviewed the clinical diagnosis of 1405 patients who died at the General Hospital of Trieste in 1974 and 1978 and who had a malignant neoplasm shown at autopsy. In 761 cases (54%) the clinical diagnosis described the site of the tumour correctly, in 267 (19%) the tumour was clinically suspected, and in 377 (27%) it was neither diagnosed nor suspected. Corresponding percentages for lung tumours were 63%, 16% and 21%.

Asnaes et al (1983), based on 266 deaths in 1974 in a Danish hospital in which autopsies were performed (85% of 312 consecutive deaths) compared cause of death as determined from clinical material only with that determined following autopsy. Based on a broad classification, the clinician's diagnosis was confirmed as incorrect in 18% of cases. This ignored differences in site and type of malignant tumour. Bronchogenic carcinoma was diagnosed in 16 cases both at autopsy and at clinical diagnosis. There were also two individuals diagnosed as having bronchogenic carcinoma only at autopsy, and one diagnosed as having it only clinically. In their introduction they note that "many studies have shown that the cause of death will be stated erroneously in about one third of all cases if only the clinical information is considered".

Goldman (1984) reviewed some of the studies correlating clinical and autopsy findings over the period 1912-1980. Citing results from 13 studies in a tabulation, the percentage of cases with missed major diagnoses with clinical relevance averaged 8.3%

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per study, with no evidence of a decline over the period. He notes that "the autopsy's unvarying percentage yield does not indicate a lack of progress, however, since bacterial pneumonia, hepatic cirrhosis, and common tumours were missed routinely in earlier eras but were rarely missed after 1970". He emphasizes the recent emergence of various infections rarely noted in prior eras as counterbalancing the improvements noted, and considers that "progress in diagnosis and treatment may allow patients to live longer and new or obscure diseases may develop that will often be missed clinically", and that a "high autopsy rate will be required if medical progress is to continue".

McFarlane et al (1986) conducted a study based on 153 necropsies in which primary lung cancer was found at the Yale-New Haven Hospital between 1971 and 1982. They collected information from the hospital records on whether the lung cancer was diagnosed in life, whether primary symptoms were present, the extent of the patient's disease at the time of diagnosis and whether the patient smoked and, if so, how many per day. The study showed that the probability of a lung cancer being diagnosed in life was significantly higher if symptoms were present and if the lung cancer was automatically widespread. The study also showed that the probability was significantly higher if the patient was a smoker, particularly a heavy smoker. Thus the proportion of cases undiagnosed before necropsy were 16% (13/79) for heavy smokers, 30% (12/40) for moderate smokers, and 57% (12/21) for non smokers. The increased probability of being diagnosed for smokers, as the authors note "suggests that smokers receive preferential consideration

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regarding the diagnosis of lung cancer". They conclude that "this detection bias can have adverse scientific consequences in depriving non-smokers of suitable therapy, in leading to falsely high estimates of the true magnitude of the smoking/lung cancer association, and in distracting etiologic attention from other agents that may cause lung cancer". The data presented allow one to estimate approximately the bias in the smoking/lung cancer relationship due to using clinical diagnoses. Thus if one wished to estimate the heavy smoking/non-smoking relative risk, a clinical study based on the cases diagnosed would observe a ratio of 66:9 deaths, instead of the true (autopsy-based) relative risk of 79:21, thus overestimating relative risk by a factor of 1.95. The authors present a table showing an odds ratio of 6.8 comparing heavy smokers and non smokers, but this is relative odds of diagnosis which is not the same thing.

Mollo et al (1986) selected a series of 970 cases with a clinical and/or post-mortem diagnosis of neoplastic disease as an underlying cause of death from autopsies performed in Turin in 1973 to 1981. There were 551 cases in which the clinical diagnosis was completely correct, 162 where the malignancy had been missed clinically, 78 where a malignancy reported clinically had not been seen at autopsy, and 179 where the clinical diagnosis had wrongly given the primary site of the malignancy. 99 cases of lung cancer were reported clinically of which 27 proved to be false positives. In addition there were a further 62 cases seen only at autopsy.

For 592 autopsies carried out at Leeds General Infirmary in 1985, Reid et al (1987) compared the clinical and autopsy diagnosis.

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The diagnoses were entered on specially designed forms, with the clinical diagnoses (usually entered before the start of the autopsy) separated into functional abnormalities, which are not directly verifiable at autopsy, and morphological abnormalities, which were compared with the autopsy diagnoses. Overall there were 432 morphological diagnoses for which the autopsy and clinical findings agreed, 168 where a clinical finding was not confirmed ("overdiagnoses"), and the 492 where an autopsy finding had not been reported clinically ("underdiagnoses"). For neoplasms, there were 55 agreements (though 4 differed as to site), 18 overdiagnoses and 28 underdiagnoses. For lung cancer, there were 11 agreements, 4 overdiagnoses and 9 underdiagnoses.

Grundmann and Menke (1991) compared autopsy and clinical diagnosis based on 4688 deaths aged 15+ autopsied in the Institute of Pathology of Münster University in 1961-1970 and 7028 autopsied in 1978-87. For the first decade, 34% of clinical diagnoses were absolutely correct, 15% were nearly correct (i.e. diagnosis widened with regard to minor details), 24% were "supplemented" (i.e. diagnosis widened with regard to essential details, but irrelevant to therapy or prognosis) and 23% were manifestly wrong. An additional 4% fell into other minor categories (e.g. main autopsy diagnosis mentioned as a side diagnosis clinically). During the second decade, 50% were correct, 15% nearly correct, 15% supplemented and 18% false, with 2% in other categories. The reduction in completely wrong diagnoses was statistically significant. For malignant neoplasms, improvements in diagnostic accuracy were also seen, with diagnoses correct in 37% and incorrect

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in 26% in 1961-1970, and correct in 47% and incorrect in 15% in 1978-1987. Of 247 lung cancers diagnosed clinically in 1961-1970, 191 (77%) were confirmed at autopsy and 56 (23%) were not. For the 432 lung cancers diagnosed in 1978-1987, 350 (81%) were confirmed and 82 (19%) were not. No results were presented for diagnoses seen at autopsy only.

Rossi et al (1991) compared clinical and autopsy diagnosis for 110 randomly selected autopsies performed in the University of Ferrara, Italy, in 1983-1987. Overall there was agreement as regards diagnosis of the primary disease in 81% of cases and of the cause of death in 58% of cases. Of 33 neoplasms diagnosed at autopsy, 4 were missed clinically, and there were a further 4 false positives. Of 17 neoplasms considered to cause death at autopsy, 3 were missed clinically, and there were a further 7 false positives. For patients dying of lung cancer it was noted that there were 3 cases where there was total agreement between autopsy and clinical diagnosis as to the site and metastases, 5 where there was partial agreement in which only the primary site or only the metastases had been diagnosed clinically, 1 false positive diagnosis, 1 false negative diagnosis and 1 unexpected diagnosis, revealed by chance at autopsy. (How this differs from a false negative diagnosis is unclear.)

Table 2 gives a summary of the main findings for lung cancer from the studies considered in this section showing the number of patients for which the lung cancer was confirmed, the number where it was seen at autopsy only and the number where the clinical diagnosis was unconfirmed. Two rates are calculated, the proportion

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TABLE 2

Difference between clinical and autopsy diagnosis of lung cancer

Principal author	Year of paper	Numbers of cancers			False negative rate (%) 100C/(A+C)	False positive rate (%) 100B/(A+B)	Under estimation factor (A+C)/(A+B)
		Clinical diagnosis		Seen at autopsy only C			
		conf A	unconf B				
Sehrt	1904	6	-	172	96.6	-	Large
Wells	1923	1	-	10	90.9	-	Large
Swartout*	1934	20	-	6	23.1	-	-
Swartout*	1940	71	-	26	26.8	-	-
Pohlen	1942	200	12	121	37.7	5.7	1.51
Munck	1952	14	2	6	30.0	12.5	1.25
O'Neal	1957	254	-	47	15.6	-	-
Waaler	1958	33	-	32	49.2	-	-
Gwynne	1965	46	2	26	36.1	4.2	1.50
Heasman	1966	227	111	190	45.6	32.8	1.23
Takeda I**	1967	179	-	166	48.1	-	-
Takeda II**	1967	1488	(305)	788	34.6	(17.0)	(1.27)
Willis	1967	43	9	28	39.4	17.3	1.37
Rosenblatt	1971	27	34	0	0.0	55.7	0.44
Bauer	1972	227	-	219	49.1	-	-
Britton	1974	9	1	7	43.8	10.0	1.60
Ehrlich	1975	25	5	9	26.5	16.7	1.30
Hartveit	1977	39	4	10	20.4	9.3	1.14
Waldron***	1977	37	11	>19	>33.9	22.9	>1.17
Hartveit	1979	71	5	35	33.0	6.6	1.39
Cechner	1980	260	38	117	31.0	12.8	1.27
Sandritter	1980	60	-	9	13.0	-	-
Cameron	1981	88	15	46	34.3	14.6	1.30
Gobbato	1982	-	-	-	37.0	-	-
Asnaes	1983	16	1	2	11.1	5.9	1.06
McFarlane	1986	103	-	37	26.4	-	-
Mollo	1986	72	27	62	46.3	27.3	1.35
Reid	1987	11	4	9	45.0	26.7	1.33
Grundmann I	1991	191	56	-	-	22.7	-
Grundmann II****	1991	350	82	-	-	19.0	-

* Respiratory cancer

** Two studies, deaths in 1948-52 (I) and in 1958-62 (II). For study II B includes only cases misdiagnosed as another cancer

*** C only includes those deaths reported clinically to be from another cancer

**** Two studies, deaths in 1961-70 (I) and in 1978-87 (II).

of autopsy diagnoses for which no lung cancer was reported clinically (false negative rate) and the proportion of clinical

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diagnoses for which no lung cancer was reported at autopsy (false positive rate). Also given is the factor by which numbers of lung cancers, as estimated clinically, would have to be multiplied to obtain numbers as estimated by autopsy (underestimation factor). For some studies the two rates and the factor cannot all be estimated, and in one study (Rossi et al., 1991), which has been omitted, none of the data can be estimated due to an inadequate description of what has been done. Studies are presented in chronological order of reporting.

It can be seen that with the striking exception of the study of Rosenblatt, whose findings bear no resemblance to anyone else's, the false negative rate typically substantially exceeds the false positive rate, though even that is quite large in some studies. The studies by Sehrt and Wells suggest (to be confirmed by further references to come) that at the beginning of the century lung cancers were much less frequently diagnosed than they are now.

2.10 Difference between necropsy and death certificate diagnosis

James et al. (1955) compared death certificate and autopsy diagnosis in 1889 patients autopsied in 12 hospitals in the Albany, New York region in 1951 and 1952. A preliminary study had shown only a very small frequency of differences in coding autopsies between the three reviewers in the study. Dividing the cause of death into 30 categories there was agreement between death certificate and autopsy diagnosis in 71.0% (1341). The number of patients classified as having died of malignant neoplasms was 372 by both sources, 37 only by autopsy, and 30 only by the death

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certificate. From a sample of 98 autopsies it was shown that differences in diagnoses were predominantly due to additional data uncovered at autopsy, only 20% of cases being due to the certifying physician making avoidable errors.

Ehrhardt et al (1959) noted that since 1945 there had been a requirement in New York City to report the results of autopsies to the vital statistics office so that the cause of death as originally reported on the death certificate could be revised accordingly. However, it was clear in 1955 that this requirement was not being held to, only 2796 reports being filed out of 10,599 deaths in which an autopsy was noted as having been done on the death certificate. Some hospitals filed no autopsy reports at all. There were also a substantial number of reports filed for deaths in which no autopsy was noted as having been done on the death certificate. Erhardt et al studied 5217 autopsy reports in the year 1956 and found that only 794 (15.2%) indicated changes in the stated cause of death. For 16,824 malignant neoplasms originally recorded as the cause of death, 186 were removed and 258 were added, yielding a net change of 0.4%. Since the impact on the final statistics was considered to be "practically negligible" the authors did not support the requirement to report autopsy results to the vital statistics office. Instead they recommended that "physicians should be encouraged to review gross autopsy findings before completing death certificates".

Rigdon and Kirchoff (1963) selected 194 cases of malignancies from autopsy records made between 1945 and 1958 at the Department of Pathology, M.D. Anderson Hospital, Houston, and then obtained the cause of death as given on the death certificate. There were 38

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